55. (New) The DSP-3 substrate trapping mutant polypeptide of claim 54 wherein the amino acid substitution at position 57 comprises an alanine residue and wherein the amino acid substitution at position 88 comprises a serine residue.

D3 Cont

REMARKS

Reconsideration of the present application in view of the above amendment and the following remarks is respectfully requested. Claims 45 and 46 are currently pending and under examination. Claim 45 has been amended to more clearly define the subject matter, without limitation, encompassed by applicants' invention. Support for the amended claim may be found in the instant specification, for example, at page 8, lines 8-24. New claims 50-55 have been added to more particularly point out and distinctly claim subject matter which applicants regard as the invention. Support for new claims 50-55 may be found in the specification, for example, at page 7, lines 15-17. Enclosed herewith is a revised Sequence Listing, which provides polynucleotide and polypeptide sequences that are identical to those disclosed in U.S. Provisional Application No. 60/142,338 (incorporated by reference in the instant application, see *infra*), and which sequences are consistent with the description in the text of the present application as filed (*see, e.g.,* present specification at page 7, lines 15-24; page 12, lines 8-18; Example 1). Substitute Figures 1-3 are also submitted herewith and are identical to Figures 1-3 in U.S. Provisional Application No. 60/142,338 (filed July 2, 1999, and incorporated by reference in its entirety into the present application, as discussed below), and are supported by the text of U.S.A.N. 60/142,338 and the present specification (*see, e.g.,* present specification at page 7, lines 15-24; page 12, lines 8-18; Example 1). Applicants respectfully submit that no new subject matter has been added.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version With Markings to Show Changes Made.**"

OBJECTION UNDER 35 U.S.C. § 132

The Examiner objected under 35 U.S.C. § 132 to the amendment filed January 11, 2002, to correct a typographical error in the specification under the caption "Cross References To Related Applications", and specifically to correct the serial number of the priority document U.S. Provisional Application No. 60/142,338 (filed July 2, 1999), asserting that the amendment introduces new matter into the disclosure of the present application. Specifically, the Examiner asserts that incorporation by reference of the subject matter of U.S.A.N. 60/142,338 introduces new matter, alleging that no support for the corrected serial number is found in any of the original application papers.

Applicants respectfully traverse this ground of objection, and submit that incorporation by reference in the present application of the subject matter disclosed in the provisional priority filing document U.S.A.N. 60/142,338 (filed July 2, 1999) does not introduce new matter into the present application because the Declaration of the Inventors in the present utility application, which is part of the original utility application, correctly recites priority to U.S.A.N. 60/142,338. A copy of the Declaration filed in the instant utility application is appended hereto.

When information submitted in an application data sheet is inconsistent with information in the Declaration or Oath of the inventors, the information filed in the latest filed document will govern (37 C.F.R. § 1.76(d)(1); *see* MPEP 601.05). The United States Patent and Trademark Office ("USPTO") has asserted that there is no support in "any of the original application papers" for the correct serial number. Applicants respectfully disagree. In the present application, the original application containing the above described typographical error was filed on April 6, 2000, and the Declaration containing the correct priority filing serial number was filed in response to a Notice to File Missing Parts at a later date, August 11, 2000. Therefore, the Declaration filed on August 11, 2000 is considered to be part of the "original application papers", and the recitation of the correct priority serial number therein satisfies the USPTO's requirements.

It is submitted that in the papers originally filed with the present utility application on April 6, 2000, the incorrect reference in the priority claim in the specification and

on the application cover sheet, as filed, to U.S.A.N. "60/142,388" were inadvertent typographical errors. The fact that these are mere typographical errors would be readily apparent by comparing the title, inventors, and attorney docket number of the present non-provisional application with the title, inventors, and attorney docket number as stated in the inventors' Declaration submitted in the present application on August 11, 2000. Moreover, the title, inventors, and attorney docket number (save for absence of the suffix "P2" denoting a provisional filing) of the present application can be matched with corresponding information fields in U.S.A.N. 60/142,338, but cannot be matched with corresponding information fields for "60/142,388" if an application having the number "60/142,388" even exists. In short, an erroneous substitution of the repeated single digit "8" for the repeated single digit "3" in the priority application serial number was properly corrected in the Declaration, such that applicants believe the priority claim of the present application to U.S.A.N. 60/142,338 has been clearly established in the record for this application.

Additionally, at the time the instant application was filed, an amendment to the specification to correct a reference to a priority document was a valid practice that was permitted under the applicable rules (37 C.F.R. § 1.78(a)(4) (*see* 37 C.F.R. Editions of 7-1-99 and 7-1-00)). Applicants respectfully submit that the amendment to the present application is in full compliance with the rules, in particular where the Declaration filed on August 11, 2000, clearly cited the correct serial number of the priority application. Applicants are therefore puzzled with respect to the assertion in the Action that the amendment of January 11, 2002, cannot be entered into the record for the present application.

A review of the files for the present application and for U.S.A.N. 60/142,338 shows that both (i) the instant utility application, and (ii) the provisional application for which the benefit of priority is claimed, have the same inventors and title, and that the claimed priority benefit fully complies with the requirements of 37 C.F.R. § 1.78(a)(4) (2001). Furthermore, and as noted above, the inventors' Declaration in the present application was timely submitted on August 11, 2000, claiming the benefit of priority of U.S. Provisional Patent Applications No.60/128,225 filed April 7, 1999, and No. 60/142,338 filed July 2, 1999.

In view of the above-described facts and the Rules under 37 C.F.R., applicants therefore respectfully submit that the error in the recitation of the provisional application serial

number in the present specification was inadvertent, and that they have complied with the procedures for properly establishing that the intended correct priority application filing serial number is readily apparent from the record of the present application, particularly in view of the properly filed Declaration. Accordingly, it is respectfully requested that the amendment to the specification, which was filed on January 11, 2002, be entered into the record for the present application. All references made herein to the Sequence Listing and to the Drawings are intended to be reference to the Sequence Listing and Drawings that are submitted herewith by amendment, as incorporated by reference.

OBJECTION TO THE SPECIFICATION

The USPTO asserts that the description of the DSP-3 polypeptide (SEQ ID NO:2) and of the disclosed substrate trapping mutants is confusing and inconsistent. Specifically, the USPTO asserts that the specification describes a substrate trapping mutant that has an aspartate residue at amino acid position 57 substituted with alanine or that has a cysteine residue at amino acid position 88 substituted with a serine, but that the residues at positions 57 and 88 disclosed in SEQ ID NO:2 are not aspartic acid and cysteine, respectively. The USPTO further asserts that on the basis of provisional application 60/128,225 (April 7, 1999), the aspartate and cysteine residues that may be mutated are located at positions 39 and 71 of SEQ ID NO:2. The USPTO notes that the amino acids located at positions 57 and 88 set forth in SEQ ID NO:2 of provisional application 60/142,338 (July 2, 1999) are aspartic acid and cysteine, respectively.

Applicants respectfully submit that the subject matter of the present invention as disclosed in the Detailed Description of the specification and Sequence Listing is consistent and clearly defined. The sequences disclosed in SEQ ID NO:1 (DSP-3 polynucleotide) and SEQ ID NO:2 (DSP-3 polypeptide), as submitted with the present amendment, are consistent with the teachings in the Detailed Description of the instant application. Specifically, the specification discloses that a DSP-3 polypeptide comprises 184 amino acids (*see, e.g.,* specification at page 12, lines 8-28; Example 1), and that the aspartate residue at position 57 or the cysteine residue at position 88 of SEQ ID NO:2 may be substituted to provide a DSP-3 substrate trapping mutant (*see, e.g.,* specification at page 7, lines 15-24). As amended herewith, applicants incorporate into

the present application the Sequence Listing that was filed in the provisional priority application U.S.A.N. 60/142,338. In the Sequence Listing, SEQ ID NO:1 and SEQ ID NO:2 disclose polynucleotide and polypeptide sequences, respectively, that are identical to the sequences disclosed in the Sequence Listing of provisional application 60/142,338 (which has been incorporated herein by reference) and do not introduce new matter. The substitute Drawings submitted herewith by amendment are also identical to Figures 1-3 in U.S.A.N. 60/142,338 (July 2, 1999), incorporated by reference in its entirety, and therefore do not introduce new matter. In view of the present amendment to substitute the Sequence Listing of incorporated U.S.A.N. 60/142,338, and the above remarks, applicants respectfully request that the objection to the specification be withdrawn.

REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

The USPTO has rejected claim 46 under 35 U.S.C. § 112, first paragraph, asserting that the claim is directed to subject matter that is not adequately described in the specification. In particular, the USPTO alleges that the applicants did not have possession of the claimed DSP-3 substrate trapping mutant polypeptides with a substitution at position 57 or at position 88 of SEQ ID NO: 2. More specifically, the USPTO asserts that the specification discloses that a DSP-3 substrate trapping mutant polypeptide has a substitution of an aspartate residue at position 57 or of a cysteine residue at position 88, but that the residues at positions 57 and 88 of SEQ ID NO: 2 of the present application are not aspartic acid and cysteine, respectively.

Applicants traverse this rejection and will demonstrate that applicants possessed the claimed invention, as disclosed in the specification and recited in the instant claims, at the time the application was filed. Applicants' invention is directed to a DSP-3 substrate trapping mutant polypeptide that differs from the sequence recited in SEQ ID NO:2 in one or more amino acid deletions, additions, insertions or substitutions at no more than 25% of the residues in SEQ ID NO:2, such that the polypeptide binds to a substrate with an affinity that is not substantially diminished relative to DSP-3, and such that the ability of the polypeptide to dephosphorylate a substrate is reduced relative to DSP-3. In certain embodiments, the invention is directed to a

DSP-3 substrate trapping mutant polypeptide that contains a substitution at position 57 or position 88 of SEQ ID NO:2.

Applicants respectfully submit that the specification as amended reasonably conveys sufficient, detailed, and relevant characteristics of the claimed polypeptides, and that a person skilled in the art would recognize that applicants possessed the claimed invention at the time the application was filed. As described in the specification, a DSP-3 substrate trapping mutant may be generated by substituting the aspartate residue at position 57 or the cysteine residue at position 88 (see specification, page 7, lines 15-24). These amino acids at the recited positions may readily be identified in SEQ ID NO:2 of the Sequence Listing as submitted in the present amendment. Applicants submit that the specification as amended clearly conveys to a person skilled in the art which amino acid residues situated at which positions in the DSP-3 polypeptide may be substituted to provide the claimed substrate trapping mutant DSP-3 polypeptide, and respectfully request that the rejection of the claim be withdrawn.

The USPTO rejected claim 45 under 35 U.S.C. § 112, first paragraph, asserting that the specification does not enable a person skilled in the art to make and use the claimed invention. In particular, the USPTO asserts that the scope of the claim is not commensurate with the subject matter enabled by the disclosure. More specifically, the USPTO alleges that while the specification is enabling for substrate trapping mutant polypeptides with a substitution at position 39 or 71 of SEQ ID NO: 2, the specification does not "reasonably provide enablement for any substrate trapping mutant of any dual specificity phosphatase having 50% identity with SEQ ID NO: 2."

Applicants respectfully disagree and will demonstrate that the specification enables a person skilled in the art to make and use the invention as claimed.

The instant specification provides explicit guidance enabling an ordinary skilled artisan to make and use the claimed polypeptides without undue experimentation. Applicants submit that the specification describes how to make and use a DSP-3 substrate trapping mutant that differs in one or more amino acid deletions, additions, insertions, or substitutions with substitutions at no more than 25% of the residues in SEQ ID NO:2. The specification discloses the DSP-3 polypeptide sequence (SEQ ID NO:2) and discloses two positions at which the amino

acid residues (position 57 and position 88 of SEQ ID NO:2) may be substituted to make a DSP-3 substrate trapping mutant (*see, e.g.,* specification, page 7, lines 15-24). A person skilled in the art can make the claimed DSP-3 substrate trapping mutants according to well known standard techniques (*e.g.*, site-directed mutagenesis) using the disclosed polynucleotide sequence (SEQ ID NO:1) encoding a DSP-3 polypeptide to design oligonucleotides for introducing a codon that encodes an amino acid other than the wildtype residue. Moreover, by using computer algorithms well known in the art, such as Align or the BLAST algorithm, a person skilled in the art can determine the percent identity of a particular polypeptide to the disclosed DSP-3 polypeptide sequence and to the disclosed DSP-3 substrate trapping mutants. As disclosed in the instant specification, a DSP-3 substrate trapping mutant variant preferably contains conservative substitutions (*see, e.g.,* specification, page 7, line 25). A conservative substitution of an amino acid may generally be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity, and/or the amphipathic nature of the residues (*see, e.g.,* specification, page 7, line 25 through page 8, line 8).

Furthermore, such person skilled in the art can readily identify or make a DSP-3 substrate trapping mutant polypeptide that differs at no more than 25% of the residues in SEQ ID NO:2 and that binds to a substrate with an affinity that is not substantially diminished relative to DSP-3, but has a reduced ability to dephosphorylate a substrate relative to DSP-3 (*see, e.g.,* specification, page 7, line 1 through page 9, line 16). Whether a DSP-3 substrate trapping mutant or a variant retains the ability to bind a substrate (*i.e.*, the K_m is not substantially diminished) but has a reduced ability to dephosphorylate a substrate (*i.e.*, the k_{cat} is reduced preferably to less than 1 per minute) may be evaluated according to methods known in the art and disclosed in the specification without undue experimentation (*see, e.g.,* specification, page 7, lines 1-24). A DSP-3 substrate trapping mutant can be analyzed for its ability to dephosphorylate a suitable substrate, such as an activated MAP-kinase, according to assays for detecting DSP-3 activity described in the specification (*see, e.g.,* specification, page 16, line 31 through page 18, line 21). Applicants submit that kinetic parameters (K_m, k_{cat}, and K_a) may readily be determined by standard methods disclosed in the instant specification and known in the art (*see, e.g.,* specification, page 7, lines 6-14, and references cited therein). Applicants respectfully submit that given the teachings of the present specification and, *inter alia*, the level

of skill in the art, performing such assays to determine whether a DSP-3 substrate trapping mutant polypeptide has reduced phosphatase activity compared with a DSP-3 polypeptide, and whether the substrate trapping mutant retains the ability to bind a substrate, would not amount to undue experimentation, but instead is merely a matter of permissible routine screening. (*In re Wands*, 858 F.2d 731, 736, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988) ("Enablement is not precluded by the necessity for some experimentation such as routine screening.").

Accordingly, applicants respectfully submit that the present application satisfies all the requirements of 35 U.S.C. § 112, first paragraph, and therefore request the rejection of the claims be withdrawn.

All of the claims remaining in the application are now allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

Ralf M. Luche and Bo Wei

SEED Intellectual Property Law Group PLLC

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MJR:sd

Enclosures:

Postcard
Copy of Declaration
Sequence Listing (same as Sequence Listing of provisional application 60/142,338)
Figures 1-3 (same as Figures 1-3 of provisional application 60/142,338)

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

The section of the application entitled "Sequence Listing" immediately after the section of the specification entitled "Abstract of the Disclosure" on page 54 has been deleted, and has been replaced with the enclosed substitute Sequence Listing.

In the Drawings:

In the Drawings, Figures 1-3 have been replaced with substitute drawings, Figures 1-3, attached hereto.

In the Claims:

Claim 45 has been amended, and new claims 50-55 have been added, as follows:

45. (Amended) A DSP-3 substrate trapping mutant polypeptide that differs from the sequence recited in SEQ ID NO:2 in one or more amino acid deletions, additions, insertions or substitutions at no more than ~~50~~25% of the residues in SEQ ID NO:2, such that the polypeptide binds to a substrate with an affinity that is not substantially diminished relative to DSP-3, and such that the ability of the polypeptide to dephosphorylate a substrate is reduced relative to DSP-3.

46. A substrate trapping mutant polypeptide according to claim 45, wherein the polypeptide contains a substitution at position 57 or position 88 of SEQ ID NO:2.

50. (New) A DSP-3 substrate trapping mutant polypeptide according to claim 45 that comprises an amino acid substitution at position 57 of SEQ ID NO:2.

51. (New) The DSP-3 substrate trapping mutant polypeptide of claim 50 wherein the amino acid substitution at position 57 comprises an alanine residue.

52. (New) A DSP-3 substrate trapping mutant polypeptide according to claim 45 that comprises an amino acid substitution at position 88 of SEQ ID NO:2.

53. (New) The DSP-3 substrate trapping mutant polypeptide of claim 52 wherein the amino acid substitution at position 88 comprises a serine residue.

54. (New) A DSP-3 substrate trapping mutant polypeptide according to claim 45 that comprises an amino acid substitution at position 57 of SEQ ID NO:2 and an amino acid substitution at position 88 of SEQ ID NO:2.

55. (New) The DSP-3 substrate trapping mutant polypeptide of claim 54 wherein the amino acid substitution at position 57 comprises an alanine residue and wherein the amino acid substitution at position 88 comprises a serine residue.

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